Determinants of care partner burden in atypical Parkinsonian syndromes: A retrospective, multi-center analysis

Jessica Shurer [a], Margaret Ivancic [b], Vanessa Nesspor [c], Maria Schmidt [c], Mingyuan Li [d], Yi-Ting Lin [d], Grant Schumock [d], Richard Xu [d], Miriam Sklerov [b,*,1], Alexander Pantelyat [c,*,1]

[a] *CurePSP, Inc., United States*
[b] *Department of Neurology, University of North Carolina at Chapel Hill, United States*
[c] *Department of Neurology, Johns Hopkins University, United States*
[d] *Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, United States*

A R T I C L E   I N F O

A B S T R A C T

Introduction: Progressive supranuclear palsy (PSP), corticobasal syndrome (CBS), and multiple system atrophy (MSA) are rare neurodegenerative diseases associated with rapid decline and require complex symptom management. Caregiving responsibilities significantly increase with progression of these atypical Parkinsonian syndromes, yet care burden in these syndromes has not been researched extensively to date.
Methods: The Zarit Burden Interview (ZBI) was used to assess burden in care partners of patients clinically diagnosed with PSP, CBS, or MSA seen in specialty interdisciplinary clinics at two academic movement disorders centers. Univariable and multivariable regression analyses were performed to evaluate cross-sectional demographic and clinical determinants of care partner burden.
Results: A total of 139 care partners completed the ZBI (59.0% PSP, 28.1% MSA, 12.9% CBS). Cohorts at both medical centers were similar across all variables. Female gender of both patients and care partners was independently associated with higher ZBI scores. Additionally, MSA-Parkinsonian type was significantly associated with lower total care partner burden compared to PSP and CBS.
Conclusion: Several determinants of higher care partner burden in atypical Parkinsonian syndromes were identified, particularly female gender and diagnosis. Healthcare professionals can consider this information when assessing individualized needs of patients and care partners and referring to disease-specific resources. Additionally, this study's methods and results highlight the potential to further explore interdisciplinary care as a means of comprehensive evaluation and support for those with atypical Parkinsonism.

1. Introduction

Progressive supranuclear palsy (PSP), corticobasal syndrome (CBS), and multiple system atrophy (MSA) are rare neurodegenerative diseases characterized by considerable disability and shortened lifespan [1,2]. Despite differences in underlying pathology, these "atypical Parkinsonian syndromes" share common diagnostic challenges, clinical courses, and care needs [3,4]. Motor parkinsonism, sleep disturbances, myoclonus, early development of more pronounced postural instability and dysphagia, anxiety and depression, poor response to dopaminergic medications, and executive dysfunction are common to all three diseases in varying degrees [3,5]. PSP is further complicated by impulsivity, lack

of insight into deficits, and gaze palsies; CBS by asymmetry, apraxia, and limb dystonia; and MSA by dysautonomia [6–8]. With no disease-modifying pharmacological and rehabilitative therapies at present, treatment for all three diseases is centered around symptom management and prevention of complications [9–12].

Because many healthcare professionals lack familiarity and comfort with diagnosing and treating atypical Parkinsonism, patients and families are often left to navigate their disease journeys without specialized care services or disease-specific educational resources [13–16]. This is complicated by the limited evidence base regarding interdisciplinary care practices and lack of documentation of the multifaceted emotional and social needs in this patient population. These are sources of

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discouragement and frustration for patients and family care partners, in addition to their uncertainty about the future and other complex psychosocial challenges [12–16].

Care partner burden is stress and other negative responses that occur in relation to the demands of caregiving for a loved one [17]. People with PSP, CBS, or MSA require increasing assistance with activities of daily living and care management over time to minimize safety risks and maintain quality of life [11]. Emerging recommendations for the provision of interdisciplinary care for Parkinsonian conditions note the importance of involving a care partner in decision-making and plans of care, as well as assessing care partner well-being over time [12,18]. Care partner burden in PSP, CBS, and MSA has been studied less extensively in comparison with other neurodegenerative conditions [13,15,16,19–21]. In Parkinson's disease and Alzheimer's disease, greater care partner burden is correlated with occurrence of falls, cognitive impairment, health-related quality of life, and advanced disease state of patients as well as anxiety, depression and poor physical health among care partners [22,23]. The existing literature on caregiving and atypical Parkinsonian syndromes has noted the positive correlation of care partner burden with both care partner anxiety and severity of patients' functional impairments [13,15,16,19–21]. This highlights a need for holistic interventions aimed at care partner burden in these neurodegenerative illnesses.

This study aims to further illuminate the determinants of burden reported by family care partners of people diagnosed with PSP, CBS, or MSA. This is the first investigation, to our knowledge, of care partner burden in atypical Parkinsonism at two different medical centers, utilizing interdisciplinary care, and across all three diagnoses.

2. Methods

2.1. Participants

The cross-sectional dataset used in this analysis included a total of 139 participants with PSP, CBS, or MSA who were seen in a specialty atypical Parkinsonism interdisciplinary clinic at one of two major academic institutions designed as CurePSP Centers of Care. Both clinics are offered monthly as half-day appointments where a patient, often with the involvement of a family member, is seen by neurology and physical, occupational and speech therapies. At Johns Hopkins University (JHU), the team also includes a nurse practitioner, a research coordinator, and music therapists, while a clinical social worker and pelvic health therapist are on the team at the University of North Carolina at Chapel Hill (UNC). The teams work together to gather patient- and care partner-reported priorities and goals, provide tailored assessments, and create a treatment plan. 78 participants were seen at JHU between 2014–2022, and 61 were seen at UNC between 2017–2022. For patients who were seen more than once, only data from the first visit were used in the analyses.

Basic demographic data included patient diagnosis, age at symptom onset, number of years since symptom onset, age at time of visit, and gender of both the patient and the care partner. The diagnosis for atypical Parkinsonian disorders was made according to accepted clinical criteria for the diagnosis of PSP, CBS, MSA-Parkinsonian type (MSA-P), and MSA-cerebellar type (MSA-C), respectively [6–8].

2.2. Care partner burden assessment

The Zarit Burden Interview (ZBI) was distributed to care partners, when available, of all patients seen in the two atypical Parkinsonism interdisciplinary clinics [24]. We used the 22-item version of the ZBI, a self-completed questionnaire that includes ordinal scale responses of 0–4, with 0 indicating lowest and 4 indicating highest burden severity [25]. The outcome measures for this study were the total ZBI score, and the care partners' overall self-assessed or perceived burden scores (ZBI question #22: "Overall, how burdened do you feel in caring for your

relative?" with answer ratings 0–4, where 0 is never and 4 is nearly always). The ZBI total score range is 0–88, where 0–21 indicates no burden, 21–40 indicates mild to moderate burden, 41–60 indicates moderate to severe burden, and above 60 indicates severe burden. Only fully completed ZBI questionnaires were included in the analysis. Data from patients who did not have an identified or participatory care partner were not included in the analysis.

2.3. Statistical analysis

Descriptive statistics (mean, median, percent, standard deviation, range) were used for the above demographic data and ZBI scores. T tests and Fisher's exact tests were used to compare demographic data as well as total and individual ZBI item scores between JHU and UNC. Two linear regression models (both with total ZBI scores as the dependent variable) were considered to quantify the effects of different predictors (independent variables) on care partner burden. Model 1 included patient gender, care partner gender, age at disease onset, years since onset, and diagnosis (PSP, CBS, MSA-P, MSA-C), while Model 2 combined MSA-C and MSA-P diagnosis ("MSA") and included an additional interaction term for patient and care partner gender pairing (M−M, M−F, F-M, F-F) to capture more complex relationships between predictors. Akaike Information Criterion (AIC) was calculated to determine the best fit model for this analysis. The best fit linear regression model was used to determine adjusted predictors of ZBI score. A multinomial regression model was used to evaluate relationships between the same predictors and scores on ZBI question 22. Because there were small numbers of some responses for question 22 (especially 3 and 4), scores were binned into "low" (0–1) and "high" (2–4) burden for analysis of perceived burden.

3. Results

3.1. Cohort characteristics

Data from a total of 139 patient-care partner pairs were analyzed (78 from JHU, 61 from UNC; 59.0 % PSP, 28.1 % MSA, and 12.9 % CBS). Patients and care partners seen at UNC and JHU did not differ significantly in gender distribution (47.4 % at JHU versus 49.2 % at UNC patients were female, and 65.2 % at JHU versus 64.1 % at UNC care partners were female), mean age at disease onset (65.2 years at JHU versus 64.1 years at UNC), and mean disease duration (4.59 years at JHU versus 4.41 years at UNC). There was a higher proportion of PSP patients from JHU compared to UNC (65.4 % versus 50.8 %, respectively), though differences in diagnosis between the centers were not statistically significant (Table 1; Fig. 1). There were 68 male–female, 46 female-male, 23 female-female, and 5 male-male pairs across the combined data sets.

Table 1
Characteristics of JHU and UNC cohorts. For patient and care partner gender and diagnosis, counts, proportions and p-value from fisher's exact test are included; for age of onset and time since onset (in years), mean, standard deviation and p-value from Welch's t-tests are included.

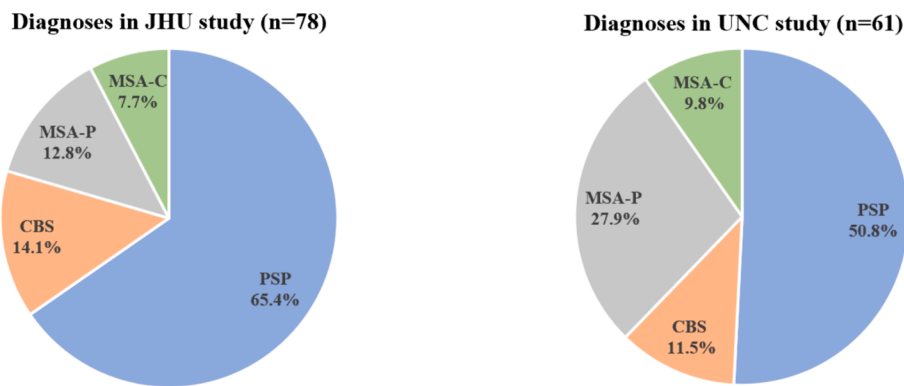|	JHU Clinic (n = 78)	UNC Clinic (n = 61)	P-value
Male Patient	41 (52.6 %)	31 (50.8 %)	0.87
Female Patient	37 (47.4 %)	30 (49.2 %)	
Male Care Partner	27 (34.6 %)	22 (36.1 %)	0.86
Female Care Partner	51 (65.4 %)	39 (63.9 %)	
PSP	51 (65.4 %)	31 (50.8 %)	0.13
CBS	11 (14.1 %)	7 (11.5 %)	
MSA-P	10 (12.8 %)	17 (27.9 %)	
MSA-C	6 (7.7 %)	6 (9.8 %)	
Age at onset (years)	65.2 (7.4)	64.1 (8.3)	0.41
Years since onset	4.59 (2.76)	4.41 (2.77)	0.70
Mean ZBI score	31.1	25.9	0.29

Fig. 1. Breakdown of diagnoses of participants seen at JHU versus UNC Clinics.

3.2. Care partner burden

The mean total ZBI scores did not differ between the two centers (mean 31.1 at JHU versus 25.9 at UNC, p = 0.29). There were no significant differences in responses to each question in the ZBI between the two centers, apart from question #17 ("Do you feel that because of the time you spend with your relative that you do not have enough time for yourself?"), where care partner burden was rated lower at JHU (p < 0.0001).

Combining JHU and UNC data, unadjusted regression modeling demonstrated that diagnosis of MSA-P and age at onset of disease were the only predictive factors for total ZBI scores (β = -8.31, p = 0.01; β = 0.31, p = 0.05, respectively). AIC for model 2 (including interaction term and combined MSA diagnosis) was 1132.53; for model 1 (no interaction term, MSA-P and MSA-C considered as separate variables), AIC was 1131.35. Therefore, model 1 was considered a better fit.

Adjusted regression analysis showed that female patient gender (β = 7.54, p = 0.02), female care partner gender (β = 6.82, p = 0.03), and MSA-P diagnosis (β = -7.85, p = 0.02) were predictive of total ZBI scores (Table 2). Since the tested predictors of total ZBI were chosen *a priori* for scientific reasons, statistical correction for multiple comparisons was not applied.

To understand the overall perceived burden of caregiving, we performed an analysis of question 22 (overall burden rating) on the ZBI. Care partners of female patients were more likely to report greater overall perceived burden (odds ratio 3.78 (Confidence interval 1.49–10.40; Fig. 2), p < 0.01).

4. Discussion

This is the first multi-site study that systematically evaluated and compared caregiving experiences across the spectrum of atypical Parkinsonian disorders in a cohort of patients seen in two specialty interdisciplinary clinics. Five determinants (patient gender, care partner gender, diagnosis, age of onset, and disease duration) were selected *a priori* and analyzed for their impact on care partner burden, as measured by the ZBI. Our findings demonstrated that gender (of both patients and care partners) had the greatest impact on burden of PSP, CBS, or MSA care partners in this cohort.

Several prior studies have evaluated care partner burden in atypical Parkinsonism. Uttl et al. assessed care partner burden by mailing questionnaires and the ZBI to 1,184 PSP patients and their care partners [19]. Results indicated that care partner burden was most related to self-reported disease severity, disease duration, and, similar to our study, female care partner gender. However, data were collected by mail, without knowledge of who completed the survey, and lacked diagnostic confirmation [19]. Kellermair et al. assessed care partner strain in both PSP and CBS [16]. Over a two-year period, care partner burden was significantly higher in PSP and female care partners were at greater risk for increased mental health challenges [16]. Our study also found significant care partner burden in PSP as compared to MSA and CBS, as well as higher care partner burden in females. Pillas et al. collected information on care partner burden by PSP phenotype through a detailed form completed by participating neurologists, which asked about the presence, type (professional or unpaid), and number of care partners, hours of care required, and most common types of required assistance [20]. Unlike in our study, care partner experience of burden was not formally assessed via a questionnaire administered to care partners [20]. Langford et al. assessed care partner experience in MSA by using the ZBI and other formalized assessments [15]. Their study, which had a small sample size of 11 care partners, found an average of mild to moderate care partner burden; this is consistent with our findings [15].

Additional research in this realm, by Kalampokini et al., assessed care partner burden across Parkinson's disease and all three atypical Parkinsonism diagnoses, limited to those considered to be in late-stage Parkinsonism (7 years and beyond) [21]. The ZBI was used to

Table 2
Results of linear modeling. The "difference" columns show change in ZBI score compared to reference group (for patient/care partner gender, diagnosis) or change in ZBI with 1 unit increase (for age of onset/time since onset).

n = 131		Unadjusted			Adjusted		
		Difference	95 % Cl	p-value	Difference	95 % Cl	p-value
Patient Gender	Male	(Reference)			(Reference)		
	Female	2.18	[−2.62,6.98]	0.37	7.54	[1.58,13.49]	**0.02**
Care Partner Gender	Male	(Reference)			(Reference)		
	Female	3.36	[−1.64,8.36]	0.19	6.82	[0.59,13.05]	**0.03**
Diagnosis	PSP	(Reference)			(Reference)		
	CBS	−1.28	[−8.52,5.97]	0.73	−1.32	[−8.43,5.79]	0.71
	MSA-P	−8.31	[−14.49, −2.14]	**0.01**	−7.85	[−14.67, −1.02]	**0.02**
	MSA-C	−1.30	[−9.91,7.30]	0.77	0.20	[−9.19,9.58]	0.97
Age of onset (years)		0.031	[0.01, 0.61]	0.05	0.22	[−0.15,0.58]	0.24
Years since onset		0.58	[−0.29,1.45]	0.19	0.75	[−0.14,1.64]	0.10

**Overall subjective burden
of female care partners**

**Overall subjective burden
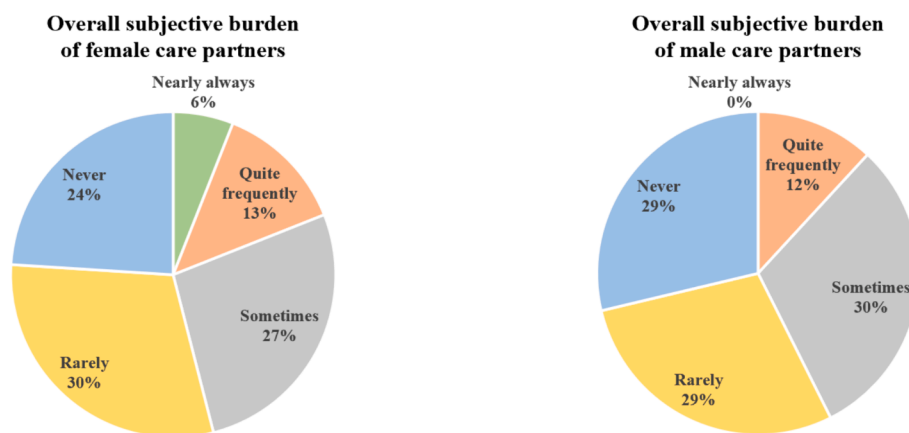of male care partners**

Fig. 2. Comparison of combined JHU-UNC responses for Question 22 of the ZBI ("overall subjective burden") by care partner gender.

evaluate care partner burden for 506 care partner participants [21]. They found that caring for a male patient was associated with higher burden in advanced Parkinsonism, which differed from our results and those of previous studies [16,18,20]. However, our study was not limited to advanced disease stages and thus cannot be directly compared to Kalampokini's study. Compared to the previously mentioned studies with larger number of participants our study is unique in comparing the care partner burden scores for 139 participants with clinically confirmed diagnosis instead of relying on self-reported or survey data.

In our study, MSA-P diagnosis was associated with lower care partner burden, though other differences in burden were not identified for other diagnoses. Increased burden of care partners of people with PSP could be related to the typically more rapid decline in cognition in this disease and in CBS, as compared to MSA [15]. The prevalence of apathy and executive dysfunction are greater in PSP than in MSA; these symptoms have been found to be associated with increased care partner burden [16,26], which may explain our findings. For example, it can take significant energy and patience for a care partner to continually prompt exercise, provide reminders about upcoming plans, or guide their loved one with significant apathy and/or executive dysfunction through the steps it takes to get ready in the morning. Additionally, as cognitive decline progresses, care partners must increasingly assist with instrumental activities of daily living and take on performance of household tasks, such as cooking, financial management, and cleaning. Care partner burden may also be affected by changes to mental health of the people they care for. People with PSP may experience more depressive symptoms than those with MSA, though they may have a similar degree of anxiety [27].

Another prominent symptom across the atypical Parkinsonian syndromes that could lead to increased care partner burden is postural instability [3]. Research in other neurological conditions, as well as early literature in PSP, has noted a relationship between falls and higher care partner burden [16,18,20]. Martínez-Villota et al. found that when comparing PSP and MSA, patients with MSA were more fearful of falling regardless of their history of falls [28]. This lack of fear of falling is suggestive of the lack of insight into imbalance and gait changes commonly experienced with PSP [28]. Cognitive impairment and impulsivity are primary contributors to risk of falls with PSP and CBS [6,3]. Therefore, PSP care partners may experience an increased sense of burden related to the need for constant monitoring in order to decrease risk behaviors and falls.

We found that gender is a significant predictor of burden in care partners of PSP, CBS, and MSA. Particularly, female gender of both patients and care partners was *independently* associated with higher burden scores. This finding reaffirms those of previous studies that reported higher burden and mental health issues among female care partners of those with atypical Parkinsonian syndromes [16,18].

Similarly, female gender has been found to be an independent predictor of reduced health-related quality of life for patients with PSP and MSA [29]. Feld et al. found that husbands were less likely to be solo care providers to their wives when daughters lived close by, but this was not the case for wives providing solo care to their husbands [30]. The increased care partner burden based on gender may be due to male care partners of female care receivers being more likely to hire outside professional help (both overall and, particularly, earlier in the disease course), which reduces overall care partner burden. Societally, men more often receive praise for providing care for their female partners because caregiving has not been traditionally viewed as a masculine role, while women providing care to their male partners are often viewed as fulfilling their designated role [30].

Our study has several important limitations. This was a retrospective study without diagnostic autopsy confirmation and did not capture socioeconomic factors, race, or mental health history of the care partner, the care partner's physical health, or the care partner's specific relationship to the care receiver. Evaluation of the impact of the relationship of the care partner to the care receiver (e.g., spouse, adult child, friend, sibling) on care burden would be interesting for future studies in this patient population, especially as they intersect with gender pairing of the patients and care partners. Furthermore, longitudinal evaluation of care partner burden and associated gender differences is warranted. We were unable to compare disease or motor severity between the centers given heterogeneity of rating scales used between diseases and between the two centers. To address this limitation, disease duration was used as a surrogate measure for disease severity, which was not found to be significantly associated with burden. In the future other modes of disease severity such as falls frequency would be interesting for a future publication. While including data from two academic medical centers was a distinct strength of this study, we acknowledge that there are differences in referral patterns and the execution of the interdisciplinary subspecialty care clinics at these two centers. Despite this, it was reassuring that there were no significant differences between proportions of specific diagnoses and other analyzed variables at the two centers.

Despite these limitations, this study highlights the importance of assessing for determinants of care partner burden in PSP, CBS, and MSA, specifically related to differences in diagnosis and gender of both patients and care partners. The strengths include a significant patient and care partner sample size and a multi-center study design. Our findings are valuable as they can guide the development of tools to aid healthcare professionals in addressing psychosocial challenges and tailoring support for the PSP, CBS, and MSA community. Additionally, our study indirectly emphasizes the importance of comprehensive care delivered through interdisciplinary clinics. Utilizing interdisciplinary care for those impacted by PSP, CBS, or MSA and their care partners may lead to earlier conversations around advance care planning, referral to disease-

specific resources, increased education on symptom management, and additional attention paid to the needs of family care partners [4,11,12,18]. In the future, further evaluation of care partner burden through this lens may improve quality of care provided by healthcare professionals caring for atypical Parkinsonism as well as the physical and mental well-being of care partners.

CRediT authorship contribution statement

Jessica Shurer: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Margaret Ivancic:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Vanessa Nesspor:** Data curation, Writing – original draft, Writing – review & editing. **Maria Schmidt:** Data curation, Writing – original draft, Writing – review & editing. **Mingyuan Li:** Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Yi-Ting Lin:** Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Grant Schumock:** Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Richard Xu:** Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Miriam Sklerov:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Alexander Pantelyat:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: JS – Director of clinical affairs and advocacy at CurePSP Foundation. MI – none. VN – none. MSc – none. ML – none. Y-TL – none. GS – none. RX – none. MSk – Research support from NIH/NIMH K23 MH132884. AP - Scientific Advisory Board, MedRhythms, Inc.; Board member, CurePSP; research support from NIH (NINDS U01 NS102035 and NIA K23 AG058981), Michael J. Fox Foundation, Parkinson's Foundation.

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